

Biological activity and pharmacological application of pectic polysaccharides: A review

Minzanova S., Mironov V., Arkhipova D., Khabibullina A., Mironova L., Zakirova Y., Milyukov V.
Kazan Federal University, 420008, Kremlevskaya 18, Kazan, Russia

Abstract

© 2018 by the authors. Pectin is a polymer with a core of alternating α -1,4-linked D-galacturonic acid and α -1,2-L-rhamnose units, as well as a variety of neutral sugars such as arabinose, galactose, and lesser amounts of other sugars. Currently, native pectins have been compared to modified ones due to the development of natural medicines and health products. In this review, the results of a study of the bioactivity of pectic polysaccharides, including its various pharmacological applications, such as its immunoregulatory, anti-inflammatory, hypoglycemic, antibacterial, antioxidant and antitumor activities, have been summarized. The potential of pectins to contribute to the enhancement of drug delivery systems has been observed.

<http://dx.doi.org/10.3390/polym10121407>

Keywords

Biological activity, Drug delivery, Modified pectin, Pectin, Pharmaceutical

References

- [1] Noreen, A.; Nazli, Z.-I.-H.; Akram, J.; Rasul, I.; Mansha, A.; Yaqoob, N.; Iqbal, R.; Tabasum, S.; Zuber, M.; Zia, K.M. Pectins functionalized biomaterials; a new viable approach for biomedical applications: A review. *Int. J. Biol. Macromol.* 2017, 101, 254-272
- [2] Yu, Y.; Shen, M.; Song, Q.; Xie, J. Biological activities and pharmaceutical applications of polysaccharide from natural resources: A review. *Carbohydr. Polym.* 2018, 183, 91-101
- [3] Bush, P. *Pectin: Chemical Properties, Uses and Health Benefits (Food Science and Technology)*; Nova Science Publishers Inc.: Hauppauge, NY, USA, 2014; ISBN 978-1633214385
- [4] Morris, V.J.; Belshaw, N.J.; Waldron, K.W.; Maxwell, E.G. The bioactivity of modified pectin fragments. *Bioact. Carbohydr. Diet. Fibre* 2013, 1, 21-37
- [5] Pérez, C.D.; De'Nobili, M.D.; Rizzo, S.A.; Gerschenson, L.N.; Descalzo, A.M.; Rojas, A.M. High methoxyl pectin-methyl cellulose films with antioxidant activity at a functional food interface. *J. Food Eng.* 2013, 116, 162-169
- [6] Mashkovskij, M. *Medicinal Preparations*, 16th ed.; Novaya Volna: Moscow, Russia, 2012; ISBN 978-5-7864-0230-9
- [7] Ho, G.T.T.; Zou, Y.-F.; Aslaksen, T.H.; Wangensteen, H.; Barsett, H. Structural characterization of bioactive pectic polysaccharides from elderflowers (*Sambuci flos*). *Carbohydr. Polym.* 2016, 135, 128-137
- [8] Ho, G.T.T.; Ahmed, A.; Zou, Y.-F.; Aslaksen, T.; Wangensteen, H.; Barsett, H. Structure-activity relationship of immunomodulating pectins from elderberries. *Carbohydr. Polym.* 2015, 125, 314-322
- [9] Ho, G.T.T.; Zou, Y.-F.; Wangensteen, H.; Barsett, H. RG-I regions from elderflower pectins substituted on GalA are strong immunomodulators. *Int. J. Biol. Macromol.* 2016, 92, 731-738
- [10] Popov, S.V.; Ovodov, Y.S. Polypotency of the immunomodulatory effect of pectins. *Biochem. Biokhimiia* 2013, 78, 823-835
- [11] Vogt, L.M.; Sahasrabudhe, N.M.; Ramasamy, U.; Meyer, D.; Pullens, G.; Faas, M.M.; Venema, K.; Schols, H.A.; Vos, P. The impact of lemon pectin characteristics on TLR activation and T84 intestinal epithelial cell barrier function. *J. Funct. Foods* 2016, 22, 398-407
- [12] Daguet, D.; Pinheiro, I.; Verhelst, A.; Possemiers, S.; Marzorati, M. Arabinogalactan and fructooligosaccharides improve the gut barrier function in distinct areas of the colon in the Simulator of the Human Intestinal Microbial Ecosystem. *J. Funct. Foods* 2016, 20, 369-379
- [13] Bräunlich, P.M.; Inngjerdina, K.T.; Inngjerdina, M.; Johnson, Q.; Paulsen, B.S.; Mabuselad, W. Polysaccharides from the South African medicinal plant *Artemisia afra*: Structure and activity studies. *Fitoterapia* 2018, 174, 182-187
- [14] Zhang, B.-Z.; Leung, W.K.; Zou, Y.-F.; Mabusela, W.; Johnson, Q.; Michaelsen, T.E.; Paulsen, B.S. Immunomodulating polysaccharides from *Lessertia frutescens* leaves: Isolation, characterization and structure activity relationship. *J. Ethnopharmacol.* 2014, 152, 340-348

- [15] Zou, Y.-F.; Barsett, H.; Ho, G.T.T.; Inngjerdengen, T.K.; Diallo, D.; Michaelsen, T.E.; Paulsen, B.S. Immunomodulating pectins from root bark, stem bark, and leaves of the Malian medicinal tree *Terminalia macroptera*, structure activity relations. *Carbohydr. Res.* 2015, 403, 167-173
- [16] Peng, Q.; Liu, H.; Shi, S.; Li, M. Lycium ruthenicum polysaccharide attenuates inflammation through inhibiting TLR4/NF-KB signaling pathway. *Int. J. Biol. Macromol.* 2014, 67, 330-335
- [17] Liu, Z.; Dang, J.; Wang, Q.; Yu, M.; Jiang, L.; Mei, L.; Shao, Y.; Tao, Y. Optimization of polysaccharides from *Lycium ruthenicum* fruit using RSM and its anti-oxidant activity. *Int. J. Biol. Macromol.* 2013, 61, 127-134
- [18] Peng, Q.; Xu, Q.; Yin, H.; Huang, L.; Du, Y. Characterization of an immunologically active pectin from the fruits of *Lycium ruthenicum*. *Int. J. Biol. Macromol.* 2014, 64, 69-75
- [19] Leivas, C.L.; Nascimento, L.F.; Barros, W.M.; Santos, A.R.S.; Iacomini, M.; Cordeiro, L.M.C. Substituted galacturonan from starfruit: Chemical structure and antinociceptive and anti-inflammatory effects. *Int. J. Biol. Macromol.* 2016, 84, 295-300
- [20] Bezerra, L.I.; Caillot, A.R.C.; Palhares, L.C.G.F.; Santana-Filho, A.P.; Chavante, S.F.; Sassaki, G.L. Structural characterization of polysaccharides from Cabernet Franc, Cabernet Sauvignon and Sauvignon Blanc wines: Anti-inflammatory activity in LPS stimulated RAW264.7 cells. *Carbohydr. Polym.* 2018, 186, 91-99
- [21] Vitaliti, G.; Pavone, P.; Mahmood, F.; Nunnari, G.; Falsaperla, R. Targeting inflammation as a therapeutic strategy for drug-resistant epilepsies: An update of new immune-modulating. *Hum. Vaccin. Immunother.* 2014, 10, 868-875
- [22] Lee, K.P.; Sudjarwo, G.W.; Kim, J.S.; Dirgantara, S.; Maeng, W.J.; Hong, H. The anti-inflammatory effect of Indonesian Areca catechu leaf extract in vitro and in vivo. *Nutr. Res. Pract.* 2014, 8, 267-271
- [23] Zhang, X.; Sun, J.; Xin, W.; Li, Y.; Ni, L.; Ma, X.; Zhang, D.; Zhang, D.; Zhang, T.; Du, G. Anti-inflammation effect of methyl salicylate 2--beta-D-lactoside on adjuvant induced-arthritis rats and lipopolysaccharide (LPS)-treated murine macrophages RAW264.7 cells. *Int. Immunopharmacol.* 2015, 25, 88-95
- [24] Lee, J.-H.; Lee, Y.-K.; Choi, Y.-R.; Park, J.; Jung, S.K.; Chang, Y.H. The characterization, selenylation and anti-inflammatory activity of pectic polysaccharides extracted from *Ulmus pumila* L. *Int. J. Biol. Macromol.* 2018, 111, 311-318
- [25] Oueslati, S.; Ksouri, R.; Pichette, A.; Lavoie, S.; Girard-Lalancette, K.; Mshvildadze, V.; Abdelly, C.; Legaul, J. A new flavonol glycoside from the medicinal halophyte *Suaeda frutescens*. *Nat. Prod. Res.* 2014, 28, 960-966
- [26] Mzoughi, Z.; Abdelhamid, A.; Rihouey, C.; Cerf, D.; Bouraoui, A.; Majdoub, H. Optimized extraction of pectin-like polysaccharide from *Suaeda frutescens* leaves: Characterization, antioxidant, anti-inflammatory and analgesic activities. *Carbohydr. Polym.* 2018, 185, 127-137
- [27] Amorim, J.C.; Vriesmann, L.C.; Petkowicz, C.L.O.; Martinez, G.R.; Noleto, G.R. Modified pectin from *Theobroma cacao* induces potent pro-inflammatory activity in murine peritoneal macrophage. *Int. J. Biol. Macromol.* 2016, 92, 1040-1048
- [28] Popov, S.V.; Markov, P.A.; Popova, G.Y.; Nikitina, I.R.; Efimova, L.; Ovodov, Y.S. Anti-inflammatory activity of low and high methoxylated citrus pectins. *Biomed. Prevent. Nutr.* 2013, 3, 59-63
- [29] Oliveira, A.F.; Nascimento, G.E.; Iacomini, M.; Cordeiro, L.M.C.; Cipriani, T.R. Chemical structure and anti-inflammatory effect of polysaccharides obtained from infusion of *Sedum dendroideum* leaves. *Int. J. Biol. Macromol.* 2017, 105, 940-946
- [30] Freysdottir, J.; Logadottir, O.T.; Omarsdottir, A.; Vikingssona, S.S.; Hardardottir, I. A polysaccharide fraction from *Achillea millefolium* increases cytokine secretion and reduces activation of Akt, ERK and NF- κ B in THP-1 monocytes. *Carbohydr. Polym.* 2016, 143, 131-138
- [31] Nascimento, G.E.; Winnischofer, S.M.B.; Ramirez, M.I.; Iacomini, M.; Cordeiro, L.M.C. The influence of sweet pepper pectin structural characteristics on cytokine secretion by THP-1 macrophages. *Food Res. Int.* 2017, 102, 588-594
- [32] Dartora, N.; Souza, L.M.; Paiva, S.M.M.; Scoparo, C.T.; Iacomini, M.; Gorin, P.A.J.; Rattmann, Y.D.; Sassaki, G.L. Rhamnogalacturonan from *Ilex paraguariensis*: A potential adjuvant in sepsis treatment. *Carbohydr. Polym.* 2013, 92, 1776-1782
- [33] Maria-Ferreira, D.; Dartora, N.; Silva, L.M.; Pereira, I.T.; Souza, L.M.; Ritter, D.S.; Iacomini, M.; Werner, M.F.P.; Sassaki, G.L.; Baggio, C.H. Chemical and biological characterization of polysaccharides isolated from *Ilex paraguariensis* A. St.-Hil. *Int. J. Biol. Macromol.* 2013, 59, 125-133
- [34] Chung, W.S.F.; Meijerink, M.; Zeuner, B.; Holck, J.; Louis, P.; Meyer, A.S.; Wells, J.M.; Flint, H.J.; Duncan, S.H. Prebiotic potential of pectin and pectic oligosaccharides to promote anti-inflammatory commensal bacteria in the human colon. *FEMS Microbiol. Ecol.* 2017, 93, 1-9
- [35] Chung, W.S.F.; Walker, A.W.; Louis, P.; Parkhill, J.; Vermeiren, J.; Bosscher, D.; Duncan, S.H.; Flint, H.J. Modulation of the human gut microbiota by dietary fibres occurs at the species level. *BMC Biol.* 2016, 14, 1-13
- [36] Liu, Y.; Dong, M.; Yang, Z.; Pan, S. Anti-diabetic effect of citrus pectin in diabetic rats and potential mechanism via PI3K/Akt signaling pathway. *Int. J. Biol. Macromol.* 2016, 89, 484-488
- [37] Chuang, E.-Y.; Lin, K.-J.; Su, F.-Y.; Mi, F.-L.; Maiti, B.; Chen, C.-T.; Wey, S.-P.; Yen, T.-C.; Juang, J.-H.; Sung, H.-W. Noninvasive imaging oral absorption of insulin delivered by nanoparticles and its stimulated glucose utilization in controlling postprandial hyperglycemia during OGTT in diabetic rats. *J. Control. Release* 2013, 172, 513-522
- [38] Xiao, Z.-Q.; Wang, Y.-L.; Yue, Y.-D.; Zhang, Y.-T.; Chen, C.-P.; Wan, L.-S.; Deng, B.; Liu, Z.-X.; Chen, J.-C. Preventive effects of polysaccharides from *Liriope spicata* var. *prolifera* on diabetic nephropathy in rats. *Int. J. Biol. Macromol.* 2013, 61, 114-120
- [39] Xu, X.; Shan, B.; Liao, C.-H.; Xie, J.-H.; Wen, P.-W.; Shi, J.-Y. Anti-diabetic properties of *Momordica charantia* L. polysaccharide in alloxan-induced diabetic mice. *Int. J. Biol. Macromol.* 2015, 81, 538-543
- [40] Palou, M.; Sánchez, J.; García-Carrizo, F.; Palou, A.; Picó, C. Pectin supplementation in rats mitigates age-related impairment in insulin and leptin sensitivity independently of reducing food intake. *Mol. Nutr. Food Res.* 2015, 59, 2022-2033
- [41] Vareda, P.M.P.; Saldanha, L.L.; Camaforte, P.N.A.; Violato, N.M.; Dokkedal, A.L.; Bosqueiro, J.R. Myrcia bella leaf extract presents hypoglycemic activity via PI3K/Akt insulin signaling pathway. *Evid. Based Complement. Alternat. Med.* 2014, 2014, 1-11
- [42] Wang, Y.; Wang, J.; Zhao, Y.; Hu, S.; Shi, D.; Xue, C. Fucoidan from sea cucumber *Cucumaria frondosa* exhibits anti-hyperglycemic effects in insulin resistant mice via activating the PI3K/PKB pathway and GLUT4. *J. Biosci. Bioeng.* 2016, 121, 36-42
- [43] Zhang, T.; Xiang, J.; Zheng, G.; Yan, R.; Min, X. Preliminary characterization and anti-hyperglycemic activity of a pectic polysaccharide from okra (*Abelmoschus esculentus* (L.) Moench). *J. Funct. Foods* 2018, 41, 19-24
- [44] Jiao, L.; Zhang, X.; Wang, M.; Li, B.; Liu, Z.; Liu, S. Chemical and antihyperglycemic activity changes of ginseng pectin induced by heat processing. *Carbohydr. Polym.* 2014, 114, 567-573
- [45] Wu, J.; Chen, M.; Shi, S.; Wang, H.; Li, N.; Su, J.; Liu, R.; Huang, Z.; Jin, H.; Ji, X.; et al. Hypoglycemic effect and mechanism of a pectic polysaccharide with hexenuronic acid from the fruits of *Ficus pumila* L. in C57BL/KsJ db/db mice. *Carbohydr. Polym.* 2017, 178, 209-220
- [46] Gyawali, R.; Ibrahim, S.A. Natural products as antimicrobial agents. *Food Control* 2014, 46, 412-429
- [47] Zhang, W.; Zhao, X.J.; Jiang, Y.; Zhou, Z. Citrus pectin derived silver nanoparticles and their antibacterial activity. *Inorg. Nano-Met. Chem.* 2017, 47, 15-20
- [48] Calce, E.; Mignogna, E.; Bugatti, V.; Galdiero, M.; Vittoriac, V.; Luca, S. Pectin functionalized with natural fatty acids as antimicrobial agent. *Int. J. Biol. Macromol.* 2014, 68, 28-32

- [49] Kutsyk, R.V.; Kosenko, S.V.; Haioshko, O.B. Pilot research of antimicrobial characteristics of pectin-containing compositions for healing wounds after teeth extraction. *Pharma Innov. J.* 2016, 5, 70-75. <http://www.thepharmajournal.com/archives/?year=2016&vol=5&issue=5&ArticleId=774>
- [50] Gupta, V.K.; Pathania, D.; Asif, M.; Sharma, G. Liquid phase synthesis of pectin-cadmium sulfide nanocomposite and its photocatalytic and antibacterial activity. *J. Mol. Liq.* 2014, 196, 107-112
- [51] Sharma, G.; Pathania, D.; Naushad, M. Preparation, characterization and antimicrobial activity of biopolymer based nanocomposite ion exchanger pectin zirconium(IV) selenotungstophosphate: Application for removal of toxic metals. *J. Ind. Eng. Chem.* 2014, 20, 4482-4490
- [52] Pathania, D.; Sharma, G.; Thakur, R. Pectin @ zirconium (IV) silicophosphate nanocomposite ion exchanger: Photo catalysis, heavy metal separation and antibacterial activity. *Chem. Eng. J.* 2015, 267, 235-244
- [53] Chauhan, N.P.S.; Gholipourmalekabadi, M.; Mozafari, M. Fabrication of newly developed pectin-GeO nanocomposite using extreme biomimetics route and its antibacterial activities. *J. Macromol. Sci. Part A Pure Appl. Chem.* 2017, 54, 655-661
- [54] Guerra-Rosas, M.I.; Morales-Castro, J.; Cubero-Marquez, M.A.; Salvia-Trujillo, L.; Martin-Belloso, O. Antimicrobial activity of nanoemulsions containing essential oils and high methoxyl pectin during long-term storage. *Food Control* 2017, 77, 131-138
- [55] Zhang, T.; Zhou, P.; Zhan, Y.; Shi, X.; Lin, J.; Du, Y.; Li, X.; Deng, H. Pectin/lysozyme bilayers layer-by-layer eposited cellulose nanofibrous mats for antibacterial application. *Carbohydr. Polym.* 2015, 117, 687-693
- [56] Minzanova, S.T.; Mironov, V.F.; Mironova, L.G.; Nizameev, I.R.; Kholin, K.V.; Voloshina, A.D.; Kulik, N.V.; Nazarov, N.G.; Milyukov, V.A. Synthesis, properties, and antimicrobial activity of pectin complexes with cobalt and nickel. *Chem. Nat. Comp.* 2016, 52, 26-31
- [57] Carneiro, A.A.J.; Ferreira, I.C.; Dueñas, M.; Barros, L.; Silva, R.D.; Gomes, E.; Santos-Buelga, C. Chemical composition and antioxidant of dried powder formulations of *Agaricus blazei* and *Lentinus edodes*. *Food Chem.* 2013, 138, 2168-2173
- [58] Wang, J.; Hu, S.; Nie, S.; Yu, Q.; Xie, M. Reviews on mechanisms of in vitro antioxidant activity of polysaccharides. *Oxid. Med. Cell. Longev.* 2016, 2016, 1-13
- [59] Yan, C.Y.; Kong, F.S.; Zhang, D.Z.; Cui, J.X. Anti-glycated and antiradicalactivities in vitro of polysaccharides from *Ganoderma capense*. *Pharmacogn. Mag.* 2013, 9, 23-27
- [60] Lima, N.S.; Oliveira, E.; Silva, A.P.; Maia, L.A.; Moura, E.G.; Lisboa, P.C. Effects of *Ilex paraguariensis* (yerba mate) treatment on leptin resistance and inflammatory parameters in obese rats primed by early weaning. *Life Sci.* 2014, 115, 29-35
- [61] Piovezan-Borges, A.C.P.; Valério-Júnior, C.; Gonçalves, I.L.; Mielniczki-Pereira, A.A.; Valduga, A.T. Antioxidant potential of yerba mate (*Ilex paraguariensis* St. Hil.) extracts in *Saccharomyces cerevisiae* deficient in oxidant defense genes. *Braz. J. Biol.* 2016, 76, 539-544
- [62] Kungel, P.T.A.N.; Correa, V.G.; Corrêa, R.C.G.; Peralta, R.A.; Soković, M.; Calhella, R.C.; Bracht, A.; Ferreira, I.C.F.R.; Peralta, R.M. Antioxidant and antimicrobial activities of a purified polysaccharide from yerba mate (*Ilex paraguariensis*). *Int. J. Biol. Macromol.* 2018, 114, 1161-1167
- [63] Hu, J.; Jia, X.; Fang, X.; Li, P.; He, C.; Chen, M. Ultrasonic extraction: Antioxidant and anticancer activities of novel polysaccharides from *Chuanxiong* rhizome. *Int. J. Biol. Macromol.* 2016, 85, 277-284
- [64] Liu, J.L.; Zheng, S.L.; Fan, Q.J.; Yuan, J.C.; Yang, S.M.; Kong, F.L. Optimisation of high-pressure ultrasonic-assisted extraction and antioxidant capacity of polysaccharides from the rhizome of *Ligusticum chuanxiong*. *Int. J. Biol. Macromol.* 2015, 76, 80-85
- [65] Huang, C.; Cao, X.; Chen, X.; Fu, Y.; Zhu, Y.; Chen, Z.; Luo, Q.; Li, L.; Song, X.; Jia, R.; et al. A pectic polysaccharide from *Ligusticum chuanxiong* promotes intestine antioxidant defense in aged mice. *Carbohydr. Polym.* 2017, 174, 915-922
- [66] Xie, T.; Kang, L.; Tang, Z.; Yang, C.; Gao, J. Physicochemical properties of enzyme and heat-moisture treated *Castanea henryi* Starches. *Nongye Jixie Xuebao/Trans. Chin. Soc. Agric. Mach.* 2015, 46, 222-227
- [67] Wei, C.; He, P.; He, L.; Ye, X.; Cheng, J.; Wang, Y.; Li, W.; Liu, Y. Structure characterization and biological activities of a pectic polysaccharide from cupule of *Castanea henryi*. *Int. J. Biol. Macromol.* 2018, 109, 65-75
- [68] Joseph, M.M.; Aravind, S.R.; George, S.K.; Varghese, S.; Sreelekha, T.T. A galactomannan polysaccharide from *Punica granatum* imparts in vitro and in vivo anticancer activity. *Carbohydr. Polym.* 2013, 98, 1466-1475
- [69] Zhai, X.; Zhu, C.; Li, Y.; Zhang, Y.; Duan, Z.; Yang, X. Optimization for pectinase-assisted extraction of polysaccharides from pomegranate peel with chemical composition and antioxidant activity. *Int. J. Biol. Macromol.* 2018, 109, 244-253
- [70] Xu, S.-Y.; Liu, J.-P.; Huang, X.; Du, L.-P.; Shi, F.-L.; Dong, R.; Huang, X.-T.; Zheng, K.; Liu, Y.; Cheong, K.-L. Ultrasonic-microwave assisted extraction, characterization and biological activity of pectin from jackfruit peel. *LWT Food Sci. Technol.* 2018, 90, 577-582
- [71] Delva, L.; Schneider, R.G. *Acerola* (*Malpighia emarginata* DC): Production, postharvest handling, nutrition, and biological activity. *Food Rev. Int.* 2013, 29, 107-126
- [72] Düsman, E.; Berti, A.P.; Mariucci, R.G.; Lopes, N.B.; Tonin, L.T.D.; Vicentini, V.E.P. Radioprotective effect of the Barbados Cherry (*Malpighia glabra* L.) against radiopharmaceutical iodine-131 in Wistar rats in vivo. *BMC Complement. Altern. Med.* 2014, 14, 1-9
- [73] Cantu-Jungles, T.M.; Iacomini, M.; Cipriani, T.R.; Cordeiro, L.M. Extraction and characterization of pectins from primary cell walls of edible açai (*Euterpeolaceae*) berries, fruits of a monocotyledon palm. *Carbohydr. Polym.* 2017, 158, 37-43
- [74] Nascimento, G.E.; Iacomini, M.; Cordeiro, L.M.C. A comparative study of mucilage and pulp polysaccharides from tamarillo fruit (*Solanum betaceum* Cav.). *Plant Physiol. Biochem.* 2016, 104, 278-283
- [75] Klosterhoff, R.R.; Bark, J.M.; Glänzel, N.M.; Iacomini, M.; Martinez, G.R.; Winnischofer, S.M.B.; Cordeiro, L.M.C. Structure and intracellular antioxidant activity of pectic polysaccharide from acerola (*Malpighia emarginata*). *Int. J. Biol. Macromol.* 2018, 106, 473-480
- [76] Chen, R.; Jin, C.; Tong, Z.; Lu, J.; Tan, L.; Tian, L.; Chang, Q. Optimization extraction, characterization and antioxidant activities of pectic polysaccharide from tangerine peels. *Carbohydr. Polym.* 2016, 136, 187-197
- [77] Rubio-Senent, F.; Rodríguez-Gutiérrez, G.; Lama-Muñoz, A.; Fernández-Bolaños, J. Pectin extracted from thermally treated olive oil by-products: Characterization, physico-chemical properties, in vitro bile acid and glucose binding. *Food Hydrocolloids* 2015, 43, 311-321
- [78] Rubio-Senent, F.; Rodríguez-Gutiérrez, G.; Lama-Muñoz, A.; García, A.; Fernández-Bolaños, J. Novel pectin present in new olive mill wastewater with similar emulsifying and better biological properties than citrus pectin. *Food Hydrocolloids* 2015, 50, 237-246
- [79] Liu, S.; Shi, X.; Xu, L.; Yi, Y. Optimization of pectin extraction and antioxidant activities from Jerusalem artichoke. *Chin. J. Oceanol. Limnol.* 2016, 34, 372-381
- [80] Eça, K.S.; Machado, M.T.C.; Hubinger, M.D.; Menegalli, F.C. Development of active films from pectin and fruit extracts: Light protection, antioxidant capacity, and compounds stability. *J. Food Sci.* 2015, 80, 2389-2396
- [81] Ayala-Zavala, J.F.; Silva-Espinoza, B.A.; Cruz-Valenzuela, M.R.; Leyva, J.M.; Ortega-Ramírez, L.A.; Carrasco-Lugo, D.K.; Pérez-Carlón, J.J.; Melgarejo-Flores, B.G.; González-Aguilar, G.A.; Miranda, M.R.A. Pectin-cinnamon leaf oil coatings add antioxidant and antibacterial properties to fresh-cut peach. *Flavour Fragr. J.* 2013, 28, 39-45
- [82] Ogutu, F.O.; Mu, T.-H. Ultrasonic degradation of sweet potato pectin and its antioxidant activity. *Ultrason. Sonochem.* 2017, 38, 726-734
- [83] Celus, M.; Salvia-Trujillo, L.; Kyomugasho, C.; Maes, I.; Loey, A.M.V.; Grauwet, T.; Hendrickx, M.E. Structurally modified pectin for targeted lipid antioxidant capacity in linseed/sunflower oil-in-water emulsions. *Food Chem.* 2018, 241, 86-96

- [84] Basanta, M.F.; Rizzo, S.A.; Szerman, N.; Vaudagna, S.R.; Descalzo, A.M.; Gerschenson, L.N.; Pérez, C.D.; Rojas, A.M. Plum (*Prunus salicina*) peel and pulp microparticles as natural antioxidant additives in breast chicken patties. *Food Res. Int.* 2018, 106, 1086-1094
- [85] Bernardi, D.M.; Bertol, T.M.; Pflanzner, S.B.; Sgarbieria, V.C.; Pollonio, M.A.R. 1-3 in meat products: Benefits and effects on lipid oxidative stability. *J. Sci. Food Agric.* 2016, 96, 2620-2634
- [86] Basanta, M.F.; Marin, A.; Leo, S.A.; Gerschenson, L.N.; Erlejan, A.G.; Tomás-Barberán, F.A.; Rojas, A.M. Antioxidant Japanese plum (*Prunus salicina*) microparticles with potential for food preservation. *J. Funct. Foods* 2016, 24, 287-296
- [87] Ramachandran, C.; Wilk, B.; Melnick, S.J.; Eliaz, I. Synergistic antioxidant and anti-inflammatory effects between modified citrus pectin and honokiol. *Evid. Based Complement. Alternat. Med.* 2017, 2017, 1-10
- [88] Wojtasik, W.; Kulma, A.; Dyminska, L.; Hanuza, J.; Zębrowski, J.; Szopa, J. Fibres from flax overproducing β -1,3-glucanase show increased accumulation of pectin and phenolics and thus higher antioxidant capacity. *BMC Biotech.* 2013, 13, 1-16
- [89] Ro, J.; Kim, Y.; Kim, H.; Jang, S.B.; Lee, H.J.; Chakma, S.; Jeong, J.H.; Lee, J. Anti-oxidative activity of pectin and its stabilizing effect on retinyl palmitate. *Korean J. Physiol. Pharmacol.* 2013, 17, 197-201
- [90] Ahn, S.; Halake, K.; Lee, J. Antioxidant and ion-induced gelation functions of pectins enabled by polyphenol conjugation. *Int. J. Biol. Macromol.* 2017, 101, 776-782
- [91] Zhang, W.; Xu, P.; Zhang, H. Pectin in cancer therapy: A review. *Trends Food Sci. Technol.* 2015, 44, 258-271
- [92] Maxwell, E.G.; Colquhoun, I.J.; Chau, H.K.; Hotchkiss, A.T.; Waldron, K.W.; Morris, V.J.; Belshaw, N.J. Rhamnogalacturonan I containing homogalacturonan inhibits colon cancer cell proliferation by decreasing ICAM1 expression. *Carbohydr. Polym.* 2015, 132, 546-553
- [93] Cheng, H.; Zhang, Z.; Leng, J.; Liu, D.; Hao, M.; Gao, X.; Tai, G.; Zhou, Y. The inhibitory effects and mechanisms of rhamnogalacturonan I pectin from potato on HT-29 colon cancer cell proliferation and cell cycle progression. *Int. J. Food Sci. Nutr.* 2013, 64, 36-43
- [94] Maxwell, E.G.; Colquhoun, I.J.; Chau, H.K.; Hotchkiss, A.T.; Waldron, K.W.; Morris, V.J.; Belshaw, N.J. Modified sugar beet pectin induces apoptosis of colon cancer cells via an interaction with the neutral sugar side-chains. *Carbohydr. Polym.* 2016, 136, 923-929
- [95] Delphi, L.; Sepehri, H. Apple pectin: A natural source for cancer suppression in 4T1 breast cancer cells in vitro and express p53 in mouse bearing 4T1 cancer tumors, in vivo. *Biomed. Pharmacother.* 2016, 84, 637-644
- [96] Lin, L.; Wang, P.; Du, Z.; Wang, W.; Cong, Q.; Zheng, C.; Jin, C.; Ding, K.; Shao, C. Structural elucidation of a pectin from flowers of *Lonicera japonica* and its antipancreatic cancer activity. *Int. J. Biol. Macromol.* 2016, 88, 130-137
- [97] Park, H.-R.; Hwang, D.; Hong, H.-D.; Shin, K.-S. Antitumor and antimetastatic activities of pectic polysaccharides isolated from persimmon leaves mediated by enhanced natural killer cell activity. *J. Funct. Foods* 2017, 37, 460-466
- [98] Ni, W.; Gao, T.; Wang, H.; Du, Y.; Li, J.; Li, C.; Wei, L.; Bi, H. Anti-fatigue activity of polysaccharides from the fruits of four Tibetan plateau indigenous medicinal plants. *J. Ethnopharmacol.* 2013, 150, 529-535
- [99] Wang, H.; Gao, T.; Du, Y.; Yang, H.; Wei, L.; Bi, H.; Ni, W. Anticancer and immunostimulating activities of a novel homogalacturonan from *Hippophae rhamnoides* L. berry. *Carbohydr. Polym.* 2015, 131, 288-296
- [100] Ogutu, F.O.; Mu, T.-H.; Sun, H.; Zhang, M. Ultrasonic Modified Sweet Potato Pectin Induces Apoptosis like Cell Death in Colon Cancer (HT-29) Cell Line. *Nutr. Cancer* 2018, 70, 136-145
- [101] Leclerc, L.; Fransolet, M.; Cote, F.; Cambier, P.; Arnould, T.; Cutsem, P.V.; Michiels, C. Heat-modified citrus pectin induces apoptosis-like cell death and autophagy in HepG2 and A549 cancer cells. *PLoS ONE* 2015, 10
- [102] Wang, X.; Lü, X. Characterization of pectic polysaccharides extracted from apple pomace by hot-compressed water. *Carbohydr. Polym.* 2014, 102, 174-184
- [103] Zhang, T.; Lan, Y.; Zheng, Y.; Liu, F.; Zhao, D.; Mayo, K.H.; Zhou, Y.; Tai, G. Identification of the bioactive components from pH-modified citrus pectin and their inhibitory effects on galectin-3 function. *Food Hydrocolloids* 2016, 58, 113-119
- [104] Prado, S.B.R.; Ferreira, G.F.; Harazono, Y.; Shiga, T.M.; Raz, A.; Carpita, N.C.; Fabi, J.P. Ripening-induced chemical modifications of papaya pectin inhibit cancer cell proliferation. *Sci. Rep.* 2017, 7, 16564
- [105] Ghalandarlaki, N.; Alizadeh, A.M.; Ashkani-Esfahani, S. Nanotechnology-Applied Curcumin for Different Diseases Therapy. *Biomed. Res. Int.* 2014, 2014, 1-23
- [106] Perteghella, S.; Crivelli, B.; Catenacci, L.; Sorrenti, M.; Bruni, G.; Necchi, V.; Vigani, B.; Sorlini, M.; Torre, M.L.; Chlapanidas, T. Stem cell-extracellular vesicles as drug delivery systems: New frontiers for silk/curcumin nanoparticles. *Int. J. Pharm.* 2017, 520, 86-97
- [107] Bai, F.; Diao, J.; Wang, Y.; Sun, S.; Zhang, H.; Liu, Y.; Wang, Y.; Cao, J. A new water-soluble nano-micelle through self-assembly pectin-curcumin conjugates: Preparation, characterization and anti-cancer activity evaluation. *J. Agric. Food Chem.* 2017, 65, 6840-6847
- [108] Chen, W.; Gou, Y.; Li, W.; Zhang, P.; Chen, J.; Wu, H.; Hu, F.; Cheng, W. Activation of intrinsic apoptotic signaling pathway in A549 cell by a pectin polysaccharide isolated from *Codonopsis pilosula* and its selenized derivative. *J. Carbohydr. Chem.* 2015, 34, 475-489
- [109] Wang, J.L.; Li, Q.Y.; Bao, A.J.; Liu, X.R.; Zeng, J.Y.; Yang, X.P.; Yao, J.; Zhang, J.; Lei, Z.Q. Synthesis of selenium-containing *Artemisia sphaerocephala* polysaccharides: Solution conformation and anti-tumor activities in vitro. *Carbohydr. Polym.* 2016, 152, 70-78
- [110] Wang, J.; Bao, A.; Wang, Q.; Guo, H.; Zhang, Y.; Liang, J.; Kong, W.; Yao, J.; Zhang, J. Sulfation can enhance antitumor activities of *Artemisia sphaerocephala* polysaccharide in vitro and vivo. *Int. J. Biol. Macromol.* 2018, 107, 502-511
- [111] Wang, J.L.; Niu, S.F.; Zhao, B.T.; Luo, T.; Liu, D.; Zhang, J. Catalytic synthesis of sulfated polysaccharides. II: Comparative studies of solution conformation and antioxidant activities. *Carbohydr. Polym.* 2014, 107, 221-231
- [112] Gaikwad, D.; Shewale, R.; Patil, V.; Mali, D.; Gaikwad, U.; Jadhav, N. Enhancement in in vitro anti-angiogenesis activity and cytotoxicity in lung cancer cell by pectin-PVP based curcumin particulates. *Int. J. Biol. Macromol.* 2017, 104, 656-664
- [113] Liu, Y.; Zheng, D.; Ma, Y.; Dai, J.; Li, C.; Xiao, S.; Liu, K.; Liu, J.; Wang, L.; Lei, J.; et al. A Self-Assembled Nanoparticles Platform Based on Pectin-Dihydroartemisinin Conjugates for Co-delivery of Anticancer Drugs. *ACS Biomater. Sci. Eng.* 2018, 4, 1641-1650
- [114] Cho, H.; Pinkhassik, E.; David, V.; Stuart, J.M.; Hastay, K.A. Detection of early cartilage damage using targeted nanosomes in a post-traumatic osteoarthritis mouse model. *Nanomed. NB* 2015, 11, 939-946
- [115] Nwakwasi, E.U.; Moharana, B.; Parthiban, M.; Preetha, S.P. Effect of pectin-tagged silver nanocomposite on A-72 cancer cell line. *Indo Am. J. Pharm. Res.* 2016, 6, 6136-6143
- [116] Suganya, K.S.U.; Govindaraju, K.; Kumar, V.G.; Karthick, V.; Parthasarathy, K. Pectin mediated gold nanoparticles induces apoptosis in mammary adenocarcinoma cell lines. *Int. J. Biol. Macromol.* 2016, 93, 1030-1040
- [117] El-Batal, A.I.; Mosalam, F.M.; Ghorab, M.M.; Hanora, A.; Elbarbary, A.M. Antimicrobial, antioxidant and anticancer activities of zinc nanoparticles prepared by natural polysaccharides and gamma radiation. *Int. J. Biol. Macromol.* 2018, 107, 2298-2311
- [118] Zhang, Y.; Sun, T.; Jiang, C. Biomacromolecules as carriers in drug delivery and tissue engineering. *Acta Pharmacol. Sin.* 2018, 8, 34-50
- [119] Marras-Marquez, T.; Peña, J.; Veiga-Ochoa, M.D. Robust and versatile pectin-based drug delivery systems. *Int. J. Pharm.* 2015, 479, 265-276

- [120] Kumar, K.V.; Choudary, P.S.; Ajaykumar, B. Design and Evaluation of Stomach-Specific Drug Delivery of Domperidone using Floating Pectin Beads. *Int. J. Drug Dev. Res.* 2013, 5, 219-228. Available online: <http://www.ijddr.in/abstract/design-and-evaluation-of-stomach-specific-drug-delivery-of-domperidone-using-floating-pectin-beads-6655.html> (accessed on 1 January 2013)
- [121] Giri, T.K.; Thakur, D.; Alexander, A.; Ajazuddin; Badwaik, H.; Tripathy, M.; Tripathi, D.K. Biodegradable IPN hydrogel beads of pectin and grafted alginate for controlled delivery of diclofenac sodium. *J. Mater. Sci. Mater. Med.* 2013, 24, 1179-1190
- [122] Saladini, B.; Bigucci, F.; Cerchiara, T.; Gallucci, M.C.; Luppi, B. Microparticles based on chitosan/pectin polyelectrolyte complexes for nasal delivery of tacrine hydrochloride. *Drug Delivery Transl. Res.* 2013, 3, 33-41
- [123] Hintzen, F.; Hauptstein, S.; Perera, G.; Bernkop-Schnürch, A. Synthesis and in vitro characterization of entirely S-protected thiolated pectin for drug delivery. *Eur. J. Pharm. Biopharm.* 2013, 85, 1266-1273
- [124] Jung, J.; Arnold, R.D.; Wicker, L. Pectin and charge modified pectin hydrogel beads as a colon-targeted drug delivery carrier. *Colloids Surf. B* 2013, 104, 116-121
- [125] Tsai, S.-W.; Yu, D.-S.; Tsao, S.-W.; Hsu, F.-Y. Hyaluronan-cisplatin conjugate nanoparticles embedded in Eudragit S100-coated pectin/alginate microbeads for colon drug delivery. *Int. J. Nanomed.* 2013, 8, 2399-2407
- [126] Pandey, S.; Mishra, A.; Raval, P.; Patel, H.; Gupta, A.; Shah, D. Chitosan-pectin polyelectrolyte complex as a carrier for colon targeted drug delivery. *J. Young Pharm.* 2013, 5, 160-166
- [127] Neufeld, L.; Bianco-Peled, H. Pectin-chitosan physical hydrogels as potential drug delivery vehicles. *Int. J. Biol. Macromol.* 2017, 101, 852-861
- [128] Miyazaki, S.; Murofushi, H.; Shimoyama, T.; Itoh, K.; Kobayashi, M.; Attwood, D. The influence of the degree of esterification on the release characteristics of in situ gelling pectin formulations for oral sustained delivery of paracetamol. *Pharm. Dev. Technol.* 2013, 18, 1259-1264
- [129] Nova, M.V.; Ratti, B.A.; Herculano, L.S.; Bittencourt, P.R.S.; Novello, C.R.; Bazotte, R.B.; Lautenschlager, S.O.S.; Bruschi, M.L. Design of composite microparticle systems based on pectin and waste material of propolis for modified L-alanyl-L-glutamine release and with immunostimulant activity. *Pharm. Dev. Technol.* 2017, 2017, 1-12
- [130] Marreto, R.N.; Ramos, M.F.S.; Silva, E.J.; Freitas, O.; Freitas, L.A.P. Impact of cross-linking and drying method on drug delivery performance of casein-pectin microparticles. *AAPS PharmSciTech* 2013, 14, 1227-1235
- [131] Badykova, L.A.; Fatykhov, A.A.; Mudarisova, R.K. Polymer Composite Films Based on Citrus Pectin for Controlled Delivery of Ceftriaxone. *Russ. J. Gen. Chem.* 2014, 84, 2004-2008
- [132] Bepeyeva, A.; Barros, J.M.S.; Albadran, H.; Kakimov, A.K.; Kakimova, Z.K.; Charalampopoulos, D.; Khutoryanskiy, V.V. Encapsulation of Lactobacillus casei into Calcium Pectinate-Chitosan Beads for Enteric Delivery. *J. Food Sci.* 2017, 82, 2954-2959
- [133] Tummalaipalli, M.; Berthet, M.; Verrier, B.; Deopura, B.L.; Alam, M.S.; Gupta, B. Drug loaded composite oxidized pectin and gelatin networks for accelerated wound healing. *Int. J. Pharm.* 2016, 505, 234-245
- [134] Chang, C.; Wang, T.; Hu, Q.; Luo, Y. Caseinate-zein-polysaccharide complex nanoparticles as potential oral delivery vehicles for curcumin: Effect of polysaccharide type and chemical cross-linking. *Food Hydrocolloids* 2017, 72, 254-262
- [135] Huang, X.; Huang, X.; Gong, Y.; Xiao, H.; McClements, J.D.; Hu, K. Enhancement of curcumin water dispersibility and antioxidant activity using core-shell protein-polysaccharide nanoparticles. *Food Res. Int.* 2016, 87, 1-9
- [136] Vityazev, F.V.; Fedyunova, M.I.; Golovchenko, V.V.; Patova, O.A.; Ipatova, E.U.; Durnev, E.A.; Martinson, E.A.; Litvinets, S.G. Pectin-silica gels as matrices for controlled drug release in gastrointestinal tract. *Carbohydr. Polym.* 2017, 157, 9-20
- [137] Krivorotova, T.; Staneviciene, R.; Luksa, J.; Serviene, E.; Sereikaite, J. Preparation and characterization of nisin-loaded pectin-inulin particles as antimicrobials. *LWT Food Sci. Technol.* 2016, 72, 518-524
- [138] Martínez, Y.N.; Cavello, I.; Hours, R.; Cavalitto, S.; Castro, G.R. Immobilized keratinase and enrofloxacin loaded on pectin PVA cryogel patches for antimicrobial treatment. *Bioresour. Technol.* 2013, 145, 280-284
- [139] Gopi, D.; Kanimozhi, K.; Kavitha, L. Opuntia ficus indica peel derived pectin mediated hydroxyapatite nanoparticles: Synthesis, spectral characterization, biological and antimicrobial activities. *Spectrochim. Acta Part A* 2015, 141, 135-143
- [140] Nisar, T.; Wang, Z.-C.; Yang, X.; Tian, Y.; Guo, Y. Characterization of citrus pectin films integrated with clove bud essential oil: Physical, thermal, barrier, antioxidant and antibacterial properties. *Int. J. Biol. Macromol.* 2018, 106, 670-680
- [141] Tian, G.; Guifang, Z.; Qiumian, Y.; Jianyuan, K.; Jinlai, O.; Zhenxia, X.; Wen, Z.; Sha, L. In vitro anticancer activity of doxorubicin-loading pectin nanoparticles. *J. Pharm. Biomed. Sci.* 2016, 6, 338-342
- [142] Minzanova, S.T.; Mironov, V.F.; Vyshtakalyuk, A.B.; Tsepaveva, O.V.; Mironova, L.G.; Mindubaev, A.Z.; Nizameev, I.R.; Kholin, K.V.; Milyukov, V.A. Complexation of pectin with macro-and microelements. Antianemic activity of Na, Fe and Na, Ca, Fe complexes. *Carbohydr. Polym.* 2015, 134, 524-533
- [143] Poset, A.M.; Lerbret, A.; Zitolo, A.; Cousin, F.; Assifaoui, A. Design of polygalacturonate hydrogels using iron (II) as cross-linkers: A promising route to protect bioavailable iron against oxidation. *Carbohydr. Polym.* 2018, 188, 276-283